Nondestructive assessment of collagen hydrogel cross-linking using time-resolved autofluorescence imaging.

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Public Summary:
We investigate the use of a fiber-based, multispectral fluorescence lifetime imaging (FLIm) system to nondestructively monitor changes in mechanical properties of collagen hydrogels caused by controlled application of widely used cross-linking agents, glutaraldehyde (GTA) and ribose. Postcross-linking, fluorescence lifetime images are acquired prior to the hydrogels being processed by rheological or tensile testing to directly probe gel mechanical properties. To preserve the sterility of the ribose-treated gels, FLIm is performed inside a biosafety cabinet (BSC). We developed correlations to quantify the relationship between mean hydrogel fluorescence lifetimes and mechanical properties of the hydrogel. In the GTA study, we observe strong and specific correlations between fluorescence lifetime and the storage and Young's moduli. Similar correlations are not observed in the ribose study and we postulate a reason for this. Finally, we demonstrate the ability of FLIm to longitudinally monitor dynamic cross-link formation. The strength of the GTA correlations and deployment of our fiber-based FLIm system inside the aseptic environment of a BSC suggests that this technique may be a valuable tool for the tissue engineering community where longitudinal assessment of tissue construct maturation in vitro is highly desirable.

Scientific Abstract:
We investigate the use of a fiber-based, multispectral fluorescence lifetime imaging (FLIm) system to nondestructively monitor changes in mechanical properties of collagen hydrogels caused by controlled application of widely used cross-linking agents, glutaraldehyde (GTA) and ribose. Postcross-linking, fluorescence lifetime images are acquired prior to the hydrogels being processed by rheological or tensile testing to directly probe gel mechanical properties. To preserve the sterility of the ribose-treated gels, FLIm is performed inside a biosafety cabinet (BSC). A pairwise correlation analysis is used to quantify the relationship between mean hydrogel fluorescence lifetimes and the storage or Young's moduli of the gels. In the GTA study, we observe strong and specific correlations between fluorescence lifetime and the storage and Young's moduli. Similar correlations are not observed in the ribose study and we postulate a reason for this. Finally, we demonstrate the ability of FLIm to longitudinally monitor dynamic cross-link formation. The strength of the GTA correlations and deployment of our fiber-based FLIm system inside the aseptic environment of a BSC suggests that this technique may be a valuable tool for the tissue engineering community where longitudinal assessment of tissue construct maturation in vitro is highly desirable.